

REMARKS

In view of the following remarks, the Examiner is requested to allow Claims 1-9 and 33-48, the only claims pending and under examination after entry of the amendments herein.

Formal Matters

Claims 1-9 and 33-38 were rejected.

Claims 1, 4 and 33 are amended. Support for these amendments can be found throughout the application as originally filed and in the following exemplary locations: paragraphs page 27, lines 2 to 24, page 32, line 14 to page 33, line 7 and Fig. 3.

New Claims 39 – 48 have been added. Support for new claims 39 – 48 can be found throughout the application as originally filed and in the following exemplary locations:

Claims 39, 42 and 45: page 13, lines 20-26, page 27, lines 2-24 and Fig. 3

Claims 40, 43 and 46: page 27, lines 11-24

Claims 41, 44 and 47: page 21, lines 15-32 and page 27, lines 2-24;

Claim 48: page 9, lines 9-19

As no new matter is added by way of these amendments, entry thereof by the Examiner is respectfully requested.

Claim Objections

Claim 1 is objected to because of the following informality: Claim 1 recites the term, "bipolymer subunit" in place of the term "biopolymer subunit."

Claim 1 is amended herein to replace the term "bipolymer subunit" with the term "biopolymer subunit." As such, Applicants respectfully request withdrawal of the objection.

Withdrawn Rejections

The Applicants wish to thank the Examiner for indicating that the rejection of Claims 1-7 and 9 under 35 U.S.C. § 102(e) as allegedly being anticipated by Cronin et al. (U.S. Patent No. 6,027,880), made in the Office Action mailed March 7, 2007, is withdrawn.

The Applicants wish to thank the Examiner for indicating that the rejection of Claim 8 under 35 U.S.C. 103(a) as allegedly being obvious over Cronin et al. (U.S. Patent No. 6,027,880) in view of Baldeschwieler et al. WO 95/25116), made in the Office Action mailed March 7, 2007, is withdrawn.

The Applicants wish to thank the Examiner for indicating that the rejection of Claims 1-9 under 35 U.S.C. 103(a) as allegedly being obvious over Hanks et al. (Methods in Enzymology, 1991, vol. 200, pages 525-532) in view of Baldeschwieler et al. WO 95/25116), made in the Office Action mailed March 7, 2007, is withdrawn.

Claim Rejections – 35 U.S.C. § 103(a)

Claims 1-9 and 33-38 are rejected under 35 USC § 103(a) as allegedly being obvious over Cantor et al. (WO 99/22025, published May 6, 1999) (hereinafter "Cantor") in view of Baldeschwieler et al. (WO 95/25116, published September 21, 1995) (hereinafter "Baldeschwieler"). The Applicants respectfully traverse the rejection.

The Patent Office bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a). *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). In order to meet its burden, the Office must first demonstrate that the prior art teaches or suggests all the claimed limitations. *See Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007), "the burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so."

As best understood by the Applicants, it is the position of the Office that Cantor discloses a microarray comprising a plurality of degenerate oligonucleotides, said degenerate oligonucleotides comprising at least one degenerate nucleotide. The Office acknowledges that Cantor does not teach a particular method of fabricating such an array. However, the Office asserts that one of ordinary skill in the art would have clearly recognized various methods for fabricating a microarray at the time the invention was made, including the method disclosed by Baldeschwieler.

According to the Office, Baldeschwieler discloses a method of fabricating an array via use of an inkjet technology, wherein the method involves the attachment of molecules onto a substrate surface, for sequential synthesis of polynucleotides, wherein the reagents are dispensed from a microdrop dispensing device. The Office acknowledges that Baldeschwieler does not teach that a "mixture" of different biopolymer subunit precursors is provided during at least one round of multiple rounds of subunit additions. However, the Office asserts that one of ordinary skill in the art would have recognized that when "growing" a degenerate polynucleotide probe on an array's surface, series of dimer additions could be utilized in addition to rounds of monomer additions. According to the Office, the deposition of dimers in fabricating the array of Cantor by the method disclosed in Baldeschwieler would have resulted in the invention as claimed.

The Applicants respectfully disagree with the reasoning and conclusions of the Office. However, solely in the interest of expediting prosecution of the instant application, the Applicants have amended independent Claims 1, 4, and 33 as follows:

Claim 1 has been amended to recite "producing a degenerate biopolymer feature location on said surface of said substrate by a method comprising providing a mixture of *two or more* different biopolymer subunit precursors to said feature location in at least one round of multiple rounds of subunit additions;"

Claim 4 has been amended to recite "producing a degenerate biopolymer feature location on said surface of said substrate by a method comprising: providing a mixture of *two or more* different biopolymer subunit

precursors to said feature location in at least one round of multiple rounds of subunit additions; and

Claim 33 has been amended to recite "producing a degenerate biopolymer feature location on said surface of said substrate by a method comprising: dispensing from a dispensing system in at least one round of multiple rounds of subunit additions a mixture comprising a predetermined ratio of *two or more* different biopolymer subunit precursors."

The Applicants submit that the proposed combination of Cantor and Baldeschwieler fail to teach or suggest at least the above elements of independent Claims 1, 4 and 33. Specifically, the combined references fail to teach or suggest *providing (or dispensing) a mixture of two or more different biopolymer subunit precursors to said feature location in at least one round of multiple rounds of subunit additions*. The Office acknowledges that these elements are not taught by Cantor (Office Action, page 3).

In fact, Cantor contains no description whatsoever regarding the actual creation of the described array. Instead, Cantor describes a simulated laboratory experiment in which a single stranded DNA of unknown sequence is sheared into overlapping oligomers 16 bases long and "hybridized" to a theoretical set of 25 "degenerate" probe groups (Cantor, page 6, lines 12 – 22). This complete lack of teaching and silence regarding the claimed elements cannot be construed as a suggestion to include the step of providing (or dispensing) a mixture of two or more different biopolymer subunit precursors to said feature location in at least one round of multiple rounds of subunit additions.

In an attempt to remedy the acknowledged deficiencies of Cantor, the Office relies on the addition of Baldeschwieler. As indicated above, the Office acknowledges that Baldeschwieler does not teach that a mixture of different biopolymer subunit precursors is provided during at least one round of multiple rounds of subunit additions. Without providing support, the Office simply asserts that one of ordinary skill in the art would have recognized that when "growing" a degenerate polynucleotide probe on an array's surface, a series of dimer additions

could be utilized in addition to rounds of monomer additions. However, even if a person of ordinary skill in art were to utilize a series of dimer additions to create an array comprising the probes of Cantor as suggested by the Office, this would still fail to result in the invention as claimed.

As used in the specification and the pending claims, "[t]he phrase 'biopolymer subunit precursor' refers to a reactive biopolymer subunit that can add to a growing chain of biopolymer subunits." The instant claims require providing or dispensing a *mixture of two or more different* biopolymer subunit precursors to said feature location in at least one round of multiple rounds of subunit additions. Thus, the claims require a *mixture of two or more different* reactive biopolymer subunits that can add to a growing chain of biopolymer subunits, an element which is neither taught nor suggested by the addition of a dimer (a single reactive biopolymer subunit) to a growing biopolymer.

The differences between the cited references and the instant claims with respect to the synthesis process are readily apparent by comparing the disclosure of Baldeschwieler with the claims as described in the instant application.

By way of example, Baldeschwieler indicates at page 13, lines 12-25 that:

In every coupling cycle, for each address on the array a number is assigned to indicate the correct synthon to be added. During the reagent delivery process, the stage raster through the addresses of the array. Tetrazole is first applied to the substrate. At each address an additional offset motion is applied to bring the correct phosphoramidite jet (A, C, G or T) in line. One or more droplets of the phosphoramidite are then dispersed. Subsequent to this a second offset motion is employed to bring the tetrazole jet in line with the address. After dispersal of the tetrazole reagent, the stage can raster to the next address for a new delivery cycle.

Thus, Baldeschwieler clearly indicates that a single type of phosphoramidite (A, C, G or T) is delivered to each address during a particular round of synthesis.

In view of the above remarks, Applicants submit that the combination of Cantor and Baldeschwieler fails to teach or suggest each and every limitation of Claims 1, 4 and 33. As such, a *prima facie* case of obviousness with respect to these claims has not been established.

Since Claims 2-3, 5-9 and 34-38 depend from Claims 1, 4 and 33, respectively, the above arguments apply equally to the rejection of Claims 2-3, 5-9 and 34-38.

Reconsideration and withdrawal of the rejection of Claims 1-9 and 33-38 under 35 USC § 103(a) are respectfully requested.

New Claims 39-48 each depend ultimately from Claim 1. As such, each of the new claims is patentable over Cantor in view of Baldeschwieler for at least the reasons discussed above.

CONCLUSION

In view of the remarks above, the Applicants respectfully submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. AGILENT 50-1078, order number 10030511-1.

Respectfully submitted,

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